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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,912	06/13/2005	**Tatsuya Ohashi**	050381	9528

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	**PAPER NUMBER**
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,912	OHASHI, TATSUYA	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2008 and 24 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 5-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 5-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/24/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The amendment filed 16 May 2008 is acknowledged and has been entered. Claims 3, 4, and 10-16 have been cancelled. Claims 1, 2, and 5-9 remain in the case.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1, 2, and 5-9 are rejected under 35 U.S.C. 112, first paragraph, for the reasons of record because the specification, while possible of being enabling for the Trk49 and Trk62 antibodies, does not reasonably provide enablement for the scope of antibodies as claimed or even for other antibodies specific for the 5a and 5b isoforms of tartrate resistant acid phosphatase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 2, and 5-9 are further rejected under 35 U.S.C. § 112, first paragraph, for the reasons of record as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the required biological materials are: (1) known and readily available to the public; (2)

reproducible from the written description; or, (3) deposited in compliance with the criteria set forth in 37 CFR §§ 1.801-1.809.

Applicant's arguments filed 16 May 2008 have been fully considered but they are not deemed to be persuasive.

Applicant urges that obtaining antibodies against enzymes is well known in the art. This is not found persuasive because the issue is not obtaining antibodies generically against enzymes, the issue, for the reasons of record, is the unpredictability of identifying relevant target/competitor pairs and appropriate specific antibodies which function for selective binding of the target substance and/or competitor in the method as claimed. As set forth, absent further guidance from applicant, one would not be assured of the ability to predictably practice the method as claimed with other target/competitor pairs or even with other than the Trk49 and Trk62 antibodies because one would have no assurance of predictably obtaining relevant reagents having the relevant immunological properties which function in the invention.

Applicant urges that the working examples can be readily applied to other systems. This is not found persuasive because it is not clear in what way the instant antibody pair functions or that the second antibody contributes anything to the working of the invention that would be applicable to any other system. The predictable reproducibility and significance of the addition of the Trk49 antibody to the assay results with the Trk69 antibody are not clear. Are the minimal changes depicted in Fig. 4 reproducible and/or significant? Binding to the Trk69 antibody appears to preserve the enzymatic activity of the (5a and) 5b isoform(s) of tartrate resistant acid phosphatase (see e.g. Ohashi et al., US 7,074,903, cols. 10-11, in view of the comparison in Janckila et al. (2001) of enzymatic activities of the 5a and 5b isoforms of tartrate resistant acid

phosphatase at pH 5.5 and 6.1 (see e.g. Fig. 3, Fig. 6A, and Table 2, showing at least a two-fold decrease in TRAcP 5a activity and approximately the same activity of TRAcP 5b with an increase in reaction pH from 5.5 to 6.1)). The Trk49 antibody can be used with the Trk69 antibody in sandwich assays (see e.g. Ohashi et al., US 7,074,903, cols. 14-15), but does this antibody bind to or inhibit the enzyme active site not bound by Trk69 and result in the differences depicted in Fig. 3 in a mechanism unrelated to the binding of fragments? Alternatively do the specificities of the Trk49 antibody for the 5a and 5b isoforms of tartrate resistant acid phosphatase differ? And, at what pH were the enzymatic assays run? These, and other, unknowns could influence the ability of one to perform the method. Notwithstanding applicant's assertions to the contrary, it is entirely unclear what, if anything, from the instant methods with the instant antibodies of unclear reactivities for the 5a and 5b isoforms of tartrate resistant acid phosphatase can be readily applied to other systems. Moreover, for the reasons set forth above, there would appear no support for the competitive substance necessarily lacking enzymatic activity as is now claimed.

Applicant urges that the specification at pages 18-19 provides a proper written description regarding the deposit of the hybridomas. This is not found persuasive for the reasons of record. Notwithstanding applicant's assertions to the contrary, it is noted that a deposit in an acceptable International Depository does not indicate that the deposit was made under the terms of the Budapest treaty and does not certify that the deposit meets the criteria set forth in 37 CFR §§ 1.801-1.809. Applicants have not shown that viable cell lines were deposited under the terms of the Budapest Treaty. Applicants have not provided the proper assurances that the cell lines

will be irrevocably and without restriction or condition released to the public upon the issuance of a patent and that the cell lines will be replaced should they ever become non-viable.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 5-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 5-8 should recite --The-- immunoassay method for proper reference to the previously recited claim components.

Applicant's arguments filed 16 May 2008 have been fully considered but they are not deemed to be persuasive. Applicant urges that it is generally acceptable for a dependent claim to begin with "A." This is not found persuasive for the reasons of record regarding proper reference to the previously recited claim components.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or

> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent,
> except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language;

Claim 9 is rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Furie et al. (US 4,769,320) for reasons of record.

Applicant's arguments filed 16 May 2008 have been fully considered but they are not deemed to be persuasive.

Notwithstanding applicant's implications to the contrary, the recitation of a minimal reaction with the competitor does not suggest no reaction therewith as would applicant's argument. Applicant is again directed to the affinities of the two antibodies for the two prothrombin forms as taught in Figs. I and II of the reference.

Applicant urges that the antibodies of the reference are individually adsorbed on carriers. This is not found persuasive because such is not excluded by the instant claim language.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claim 9 is rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Davalian et al. (US 6,190,873) for reasons of record in the prior rejection of the similar subject matter of this claim.

Applicant's arguments filed 16 May 2008 have been fully considered but they are not deemed to be persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the feature upon which applicant relies (i.e., the second antibody has affinity for both of the target/competitor pair) is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Notwithstanding applicant's assertions to the contrary, the reference teaches a variety of immunoassay formats involving specific binding pair members immobilized on a solid support.

Claims 1, 2, and 6-9 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Halleen et al. (US 6,248,544) for reasons of record in the prior rejection of the similar subject matter of these claims.

Claims 1, 2, and 6-9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Halleen et al. (US 6,248,544) in view of Carlsson et al. (US 6,737,278) for reasons of record in the prior rejection of the similar subject matter of these claims.

Applicant's arguments filed 16 May 2008 have been fully considered but they are not deemed to be persuasive.

Applicant's arguments were not found persuasive because it appears that applicant is confusing the alternative sandwich embodiment of the disclosure of Halleen et al. with that as applied in the rejection of record (e.g.: col. 6, lines 16-22; cols 8-9, Examples 2-3) wherein the antibodies are immobilized on solid phases and sequentially reacted with sample to bind the 5a form to the 5a-specific antibody and then the unbound 5b form to the tartrate resistant acid phosphatase-specific antibody for determination of bound enzymes by enzymatic assays performed at different pH values. The antibody specific for both forms is, as set forth in the rejection of record, clearly the first antibody of the method as instantly claimed.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the feature upon which applicant relies (i.e., the second antibody has affinity for both of the target/competitor pair) is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant urges that one would not know how to combine the flow matrix method and kit of Carlsson et al. with the reagents and method taught in Halleen et al. for the determinations of the isoforms of tartrate resistant acid phosphatase. This is not found persuasive for the reasons of record. The examiner would note that, for the reasons of record as set forth, it would have been obvious to one of ordinary skill in the art to have combined the teachings of the references and to have immobilized the anti-tartrate resistant acid phosphatase **5a** isoform antibodies taught in Halleen et al. in the separation zone of Carlsson et al. to bind the 5a isoform for detection of the other heteroform, the tartrate resistant acid phosphatase **5b** isoform, in the detection zone of

Carlsson et al. with the immobilized anti- tartrate resistant acid phosphatase antibodies and enzyme substrate as taught in Halleen et al.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR REPLY TO THIS FINAL ACTION IS SET TO EXPIRE **THREE MONTHS** FROM THE MAILING DATE OF THIS ACTION. IN THE EVENT A FIRST REPLY IS FILED WITHIN **TWO MONTHS** OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE **THREE-MONTH** SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR REPLY EXPIRE LATER THAN **SIX MONTHS** FROM THE MAILING DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 11 a.m. to 7 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun, Ph.D.
Examiner, Art Unit 1641
September 4, 2008

/Mark L. Shibuya, Ph.D./
Supervisory Patent Examiner, Art Unit 1641